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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,699	06/14/2002	Ikuo Nishimoto	082376-000000US	2315

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EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,699	NISHIMOTO, IKUO	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-21* is/are pending in the application.

4a) Of the above claim(s) *3 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-8 and 10-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/18/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 9/23/2005 in which claims 2, 8 and 12 were amended and new claims 20-21 were added. Claims 3 and 9 stand withdrawn as being drawn to a non-elected invention. Claims 2, 4-8, 10-21 are under consideration in the instant application. Claims 2-21 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

Acknowledgement is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). However, it is noted that there is no English translation of either foreign patent document, thus an accurate determination of the priority claim in terms of support for the invention cannot be made regarding those documents. As a result, priority is only granted as far as the filing date of the PCT/JP00/06313 application.

Response to Arguments

Applicant argues in the papers filed 9/23/2005 that the Examiner need not make any comment on whether Applicant is entitled to the claimed priority date because the "three

references cited by the Examiner [in the Office Action of 3/25/2005] predate the earliest priority document" (page 6). In support of this argument, Applicant cites MPEP at §201.15.

The Examiner agrees with Applicant insofar as Applicant need not provide a translation unless an intervening reference is found and insofar as MPEP §201.15 provides support for this assertion. However, the Examiner notes that there were actually four references, not three, cited in the Office Action of 3/25/2005. The Slamon reference (U.S. Patent 6,770,477) of the cited Office Action has as its effective filing date October 6, 1999, which makes it an intervening reference for the instant application which claims priority from a PCT application filed on 9/14/2000 to two foreign patent applications, one of which was filed on 9/17/1999. Therefore, without a translation of the foreign patent document, priority is only granted as far as the filing date of the PCT/JP00/06313 application.

Claim Rejections - 35 U.S.C. §102

Claims 2, 4-8, 10-17 and 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Vito *et al.* (IDS reference AG; see entire document; henceforth Vito). This rejection is maintained for reasons of record in the Office Action mailed

3/25/2005 and slightly altered in order to take into consideration Applicant's amendment filed 9/23/2005.

Vito teaches the expression of a cDNA library in mice T-cell hybridoma (3DO) cells that are undergoing programmed cell death (PCD) induced by T-cell receptor (TCR) cross-linking (see for example page 521, left column, first paragraph). Vito further teaches the identification of six cDNA clones having a suppressive effect on the PCD phenotype of the 3DO cells, designated ALG-1 through ALG-6 (see for example page 521, left column second paragraph). It is important to note that the cDNA library is obtained from cells undergoing PCD, thus these nucleic acids are identical to those obtained from an organ undergoing cell death, absent evidence to the contrary. This includes brain and nerve tissue, as well as tissue isolated from Alzheimer's disease afflicted organs. Vito also teaches the method above comprising obtaining the nucleic acids expressed in the tissue of the organism suffering from the disorder and constructing the library of nucleic acids therefrom (see section entitled "References and Notes" on page 524, especially No. 4).

Claims 2, 4-8, and 10-17 were rejected under 35 U.S.C. 102(b) as being anticipated by Guo *et al.* (IDS reference AF; see entire document). Claims 2, 4-8, and 10-17 were also rejected

under 35 U.S.C. 102(b) as being anticipated by Giambarella *et al.* (EMBO J 16:4897-4907, 1997). These rejections are withdrawn due to Applicant's amendment and arguments regarding these rejections are therefore not included in the response below.

Response to Arguments

Applicant argues that the rejection of claims 2, 4-8 and 10-17 under 35 U.S.C. §102(b) should be withdrawn for the following reasons:

1. Applicant argues that the Examiner has provided no legal basis to support the position that the recited source of the nucleic acids in the claims can be ignored in a process claim. Applicant's argument stems from the assertion, argued below, that Applicant believes that the cDNA library obtained from cells undergoing PCD in Vito are not identical to those nucleic acids obtained from an organ undergoing cell death. Furthermore, Applicant argues that the source of the nucleic acids need not be considered in determining novelty in "product-by-process" claims but asserts that the claims pending are "process-by-process" claims and that, accordingly, the source of the nucleic acids of the claims warrants consideration in the determination of their novelty.

2. Applicant has amended claims 2 and 8 now to specify that a library of nucleic acids, obtained from or synthesized from nucleic acids expressed in the tissue showing cell death as a pathological feature of the disorder, is expressed in a population of cells. Applicant argues that the present claims are directed to a library of nucleic acids derived from cells expressing genes during disease pathogenesis in an *in vivo* context and that, in contrast, Vito discloses the expression of a cDNA library constructed from mRNA of an *in vitro* cultured cell line. Furthermore, Applicant notes that while any particular nucleic acid obtained from the cells of Vito may or may not be identical to a nucleic acid obtained from a cell of a tissue obtained from an organ undergoing cell death as a pathological feature of a disorder, a library of expressed nucleic acids as disclosed by Vito would not be identical to a library of expressed nucleic acids as recited in the present claims, i.e. the library of nucleic acids obtained from or synthesized from nucleic acids expressed *in vivo* in a tissue obtained from a disease organ would show structural variation with respect to the frequency of expressed sequences as well as the identity of certain sequences as compared to a library constructed from the immortalized 3DO cell line cultured *in vitro*.

3. Applicant further argues that the conditions used in Vito for inducing apoptosis in 3DO cells are not substantially representative of conditions that would be encountered physiologically *in vivo*. Applicant notes that the 3DO cells of Vito were stimulated with anti-CD3ε 2C11 antibody, but that under physiological conditions several factors modulate apoptotic cell death in T lymphocytes, including e.g., interleukins, glucocorticoid hormones, and adhesion receptors. Applicant recites that cells showing such differences in apoptotic activation would be expected to show differences in gene expression patterns. Applicant argues for this reason and for the reasons above, the cDNA library of Vito is structurally and functionally distinguishable from the nucleic acid library recited in the present claims.

4. Applicant argues that the presence of additional factors *in vivo* that modulate apoptosis is particularly relevant to the present invention. Applicant argues that in disorders accompanying cell death, cell death does not always occur in all cells contained in the affected areas, and that tissues in the vicinity of the affected area may sufficiently express suppressor genes preventing the development of pathological symptoms. Applicant asserts that by using such tissues to construct a nucleic acid library, a library condensed for

disease-suppressors can be obtained. Applicant further notes that the skilled artisan would not reasonably view in vitro cultured 3DO cells, artificially stimulated only through the TcR with an anti-CD3ε 2C11 antibody, as containing physiologically relevant disease-suppressing factors to the same degree as tissue actually obtained from an organ showing cell death as a pathological feature of a disorder.

Applicant's arguments have been fully considered and are respectfully found unpersuasive for the reasons set forth below.

Regarding Applicant's first argument that the Examiner has provided no legal support for the assertion that the source of the cDNA in the presently claimed invention can be ignored, Applicant is respectfully reminded that the source of the cDNA in the presently claimed invention was indeed considered and accorded the appropriate patentable weight in the context of the claim. The claims are not, as the Applicant argues, process-by-process claims, but rather process claims with a product-by-process claim embedded in them. Because there is not structural or functional variation conveyed upon the nucleic acids obtained from cells undergoing PCD with respect to the same kind of cells not undergoing PCD, be they from T cells *in vitro* or nerve cells *in vivo*, the nucleic acids of Vito are identical to those obtained from an organ undergoing cell death.

Regarding Applicant's second argument, amendment of the claims to specify that a library of nucleic acids, obtained from or synthesized from nucleic acids expressed in the tissue showing cell death as a pathological feature of the disorder, is expressed in a population of cells, does not further differentiate the nucleic acids of Vito from those of the instant claims. Furthermore, Vito teaches a library of cDNAs and Applicant admits this to be true (see Vito column 1, first paragraph as well as page 8 of the remarks filed by Applicant on 9/23/2005). Vito also teaches nucleic acids obtained from or synthesized from nucleic acids expressed in a tissue of an organism suffering from a disorder because these nucleic acids are the same as those obtained from cultured 3DO cells undergoing PCD. Vito also teaches the library of cDNAs expressed in a population of cells (see for example page 521, left column, first paragraph). Applicant's argument that while any particular nucleic acid obtained from the cells of Vito may or may not be identical to the nucleic acids obtained from a cell of a tissue obtained from an organ undergoing cell death as a pathological feature of the disorder, a library of expressed nucleic acids as disclosed by Vito would not be the same as a library of expressed nucleic acids as recited in the present claims is unsubstantiated. The nucleic acids of the present

claims and those of Vito are chemically the same and differ only in amount. The frequency of the expressed sequences does not change the nature of those sequences. Furthermore, if several or even a few of the nucleic acids expressed in Vito are the same as those of the presently claimed invention (which, absent evidence to the contrary, they are), then the nucleic acids of Vito read on the present claims.

Applicant's third argument that the conditions used in Vito for inducing apoptosis in 3DO cells are not substantially representative of conditions that would be encountered physiologically *in vivo* is not germane for the reasons described above, i.e. that genes expressed are the same and source of the expressed genes in the instant claims, upon consideration, is not granted patentable weight. The conditions within which the cells were found upon obtaining or synthesizing the nucleic acids does not change the chemical nature of the expressed nucleic acids.

Applicant's fourth argument that by using a library of nucleic acids obtained from nucleic acids expressed in a tissue of an organism suffering from a disorder, a library condensed for disease-suppressors can be obtained has also been considered. There is nothing in the claims to indicate that the nucleic acids obtained from a diseased organ have any structural

or functional variation from nucleic acids obtained from a normal organ. Indeed, the nucleic acids obtained from diseased organs will certainly contain nucleic acids from non-diseased cells, which would be identical to those obtained from normal cells. As such, it appears that the nucleic acids obtained from normal cells read on the nucleic acids to be expressed in the instant claims. Therefore, absent evidence to the contrary, this library would, in fact, be the same as that obtained in Vito for the reasons already recited above.

Claim Rejections - 35 USC § 103

Claims 2, 4-8, 10-17, 18-19* and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vito (as recited above in the rejection of claims 2, 4-8, 10-17 and 20-21 under 102(b)) in view of Slamon *et al.* (US Patent No. 6,770,477; see entire document, henceforth Slamon). Note-* indicates the claims that are specifically rejected by the combination of references. This rejection is maintained for reasons of record in the Office Action mailed 3/25/2005 and slightly altered in order to take into consideration Applicant's amendment filed 9/23/2005.

Vito teaches all of the elements as set forth above, specifically the expression of a library of nucleic acids in a

cell, followed by the isolation of a plurality of nucleic acids having the ability to suppress the cell death phenotype of the cell. Specifically, Vito teaches the isolation of six cDNA clones having the ability to suppress the cell death phenotype.

Vito does not teach the cross-hybridization of the six suppressors to identity which of the suppressors is non-redundant.

Slamon teaches the identification of 43 C clones and 36 H clones, and the cross-hybridization of these sequences to determine redundancy within the isolated clones prior to secondary screening (see for example, column 47, lines 10-15). Following the cross-hybridization, 7 non-redundant C clones and 12 non-redundant H clones were identified (see for example, column 47, lines 15-16). Thus, Slamon teaches that the use of cross-hybridization can be an effective tool in reducing the number of clones prior to further characterization.

It would have been obvious to combine the cross-hybridization technique of Slamon with the screening technique of Vito because both methods identity a plurality of clones that may be redundant in content, and Applicant clearly indicates that the use of such cross-hybridization techniques for the purpose of identifying non-redundant groups of nucleic acids was well-known to the skilled artisan prior to the filing date of

the instant application (see for example, page 9, second paragraph of Applicant's response).

The skilled artisan would have been motivated to combine the method of Vito and the method of Slamon because it is desirable to reduce the number of clones to be further characterized to prevent redundant characterization of the same clone; as evident from Slamon, the cross-hybridization technique is useful in determining the unique members of a group of isolated clones, and this technique could be used to determine whether the ALG clones 1-6 of Vito are unique and require individual characterization, or if one or more clones is redundant, thus reducing the number of characterizations required for each of the unique clones.

Absent evidence to the contrary, and given the well-known nature of the cross-hybridization technique for the purpose of identifying non-redundant groups of nucleic acids, the skilled artisan would have had a reasonable expectation of success when combining the cited methods of Vito and Slamon.

Response to Arguments

Applicant argues that the rejection of claims 2, 4-8, 10-17 and 18-19 under 35 U.S.C. §103(a) should be withdrawn because the rejection is obviated in view of the amendments and remarks

set forth in response to the rejection in view of Vito. These arguments, including both the amendments to the claims as well as the remarks regarding the rejection in view of Vito have been addressed above.

Conclusion

No claims are allowed.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter A. Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office.)

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

December 9, 2005

JAMES KETTER
PRIMARY EXAMINER